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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,500	07/11/2003	Henning Ralf Stennicke	6510.200-US	3991

23650 7590 06/28/2006

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PATENT DEPARTMENT
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EXAMINER	
SCHNIZER, HOLLY G	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/617,500	STENNICKE ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *8,9,11-16,18-26 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,17 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/25/04, 1/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, with the species election of A is catalytically inactivated FVIIa, LM is Phe-Phe-Arg Chloromethylketone, and C is melphalan in the reply filed on 4/6/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of the Claims

Claims 1-27 and 29-31 are pending. Claims 8-9, 11-16, 18-26, and 29-31 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7, 10, 17, and 27 as they read on the elected species have been considered in this Office Action. It is noted that Applicants indicated claims 19-26 as reading on the elected species. However, these claims identify LM as a disulfide bond which is not the Phe-Phe-Arg Chloromethylketone identified as the elected group. Thus, claims 19-26 are withdrawn from consideration.

Domestic Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/404,567, filed 8/19/02. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an

application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge

under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 10, 17, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (Proc. Natl. Acad. Sci. (1999) Vol. 96, pp. 8161-8166; ref. cited in IDS filed 1/26/04) in view of US Patent No. 5,997,864 (the 864 patent) and Pietersz et al. (Adv. Immunol. (1994) Vol. 56, pp. 301-387).

Hu et al. teaches a compound having the formula A-(LM)-C wherein a comprises an inactive factor VII (FVIIa) (a tissue factor antagonist), and C comprises the Fc effector domain of human IgG1 (an antibody that induces an immune response against the targeted cells) (see p. 8161). Hu et al. teaches that the FVIIa was mutated to inhibit initiation of the coagulation pathway without affecting the affinity for tissue factor (p. 8161). Hu et al. teaches that the conjugates are to be used as immunotherapy treatment for cancer (a pharmaceutical use).

Hu et al. does not teach that the factor VIIa is inactivated with Phe-Phe-Arg chloromethylketone (FFR-cmk) or that the cytotoxic domain is melphalan.

However, FVIIa inactivated with FFR-cmk is considered an art recognized equivalent to an active site mutated FVIIa. Both the active site mutant of Hu et al. and FVIIa-FFR-cmk are made to eliminate coagulation activity while maintaining tissue factor binding ability. The '864 patent provides evidence that catalytic site mutants of FVIIa (such as that taught in Hu et al.) and FVIIa inhibited at its active site by chemical derivatization (including FFR-cmk) were well known functional equivalents (see the '864 patent, col. 9, lines 50-65).

Pietersz et al. provides a review of targeted chemotherapy using conjugates containing targeting domains and cytotoxic domains. The review provides evidence that making such conjugates was routine in the art at the time of the invention and various cytotoxic agents could be selected equivalently for the cytotoxic domain. Tables I (p. 302) and III (p. 313) show that melphalan was well known as a cytotoxic drug that could be conjugated to a targeting domain so that the drug could be targeted to specific cells.

It is prima facie obvious to substitute one equivalent component for another (see MPEP 2144.06). Inactive FVIIa was a well known targeting agent used in conjugates to deliver cytotoxic agents to specific cells (see Hu et al.) and melphalan was well known cytotoxic agent that could be used in conjugates with a targeting domain to be delivered to specific cells. Hu et al. and Pietersz et al. suggest that a wide variety of different combinations of targeting domain and cytotoxic agent had been used successfully. Moreover, the '864 patent provides evidence that active site mutants of FVII are functionally equivalents of FVII catalytically inactivated at the active site with a derivative such as FFR-cmk. Therefore, one would have had a reasonable expectation of

success and it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute FVIIa-FFR-cmk for the inactivated FVIIa and melphalan for the antibody in the conjugate of Hu et al. Doing so would have been a selection of a known material based on its suitability for its intended use (see MPEP 2144.07) and thus the claims are considered prima facie obvious.

Claimed Genus is anticipated The following rejection shows that the claimed genus is anticipated (as well as being obvious as discussed above) by the prior art. Therefore, species additional to the elected species will not be considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (Proc. Natl. Acad. Sci. (1999) Vol. 96, p. 8161-8166; cited in IDS filed 1/26/04).

Hu et al. teaches a compound having the formula A-(LM)-C wherein A comprises an inactive factor VII (FVIIa) (a tissue factor antagonist), and C comprises the Fc effector domain of human IgG1 (an antibody that induces an immune response

against the targeted cells) (see p. 8161). The compositions of Hu et al. containing the conjugates were administered to mice and thus these compositions are considered pharmaceutical.

Conclusions

No Claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday-Thursday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

June 22, 2006

HOLLY G. SCHNIZER, PH.D.
PATENT EXAMINER